

A petition for an extension of time of three (3) months for responding to the outstanding Office Action and the appropriate fee authorization is enclosed herewith.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is entitled "VERSIONS WITH MARKINGS TO SHOW CHANGES MADE."

Applicants will file a supplemental response enclosing certified copies of the priority applications to fulfill the requirements of 35 USC 119(b).

The Examiner stated that the application is not fully in compliance with the sequence rules, 37 CFR §1.821-1.825 because the specification does not recite the appropriate sequence identifiers. Applicants respectfully submit that the application is in compliance. However, in order to expedite examination of this case, Applicants will submit under separate cover, a new sequence listing including the sequence set forth on page 13 with the amendments to the specification at that time..

The Examiner has indicated that claim 20 is withdrawn from further consideration to the extent that it is drawn to a non-elected invention. Claim 20 has been amended to remove the dependency on claim 19 to obviate this issue.

Claim 6 stands objected to under 37 CFR 1.75(c) as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicants respectfully disagree with the Examiner's position and objection. It is clear that the amino acids set forth in SEQ ID NOs 35-55 are examples of peptides that have an amino acid sequence derived from SEQ ID NO:1 by deletion, substitution or insertion of 1 to 5 amino acid residues. In order to expedite prosecution, however, Applicants have amended claim 6 to be an independent claim, as suggested by the Examiner.

Claims 1-8, 18, 20, 24 stand rejected under 35 USC 101 as directed to non-statutory subject matter. Applicants respectfully disagree. However, in order to expedite prosecution of this application, claim 1 has been amended to recite an isolated peptide, as suggested by the Examiner to refer to all natural and synthetic peptides having the sequences set forth in the claims. Therefore, Applicants respectfully request that this rejection be reconsidered and withdrawn.

Claims 1, 2, 4-6, 18, 20, 24 stand rejected under 35 U.S.C. 112, first paragraph. Applicants respectfully traverse this rejection.

It is the Examiner's position that the specification is enabling for a polypeptide comprising the amino acid sequence of SEQ ID NO: 1. However, the Examiner argues, it does not reasonably provide enablement for a deleted or substituted variant thereof. Applicants respectfully disagree with the Examiner's position.

It is the Examiner's position that predicting structure and therefore function, from primary amino acid sequence data is extremely complex and there are no algorithms for predicting the structure of a given protein from its amino acid sequence alone. The Examiner cites Bowie, page 1306, column 1, full paragraph 1, and Ngo, page 433 [sic], full paragraph 1, and page 492, full paragraph 2. Applicants respectfully direct the Examiner to Ngo and the fact that there is no page 433 in this reference. Applicants' respectfully submit that these references actually discuss methods of analysis of amino acid substitutions to reduce the complexity of sequences and show aspects of structure and function (Bowie) and that one cannot rule out the existence of a protein-predictions algorithm (Ngo). In fact, Bowie supports the idea that a protein of interest may be a member of a family of related sequences. Page 1310.

Regardless, contrary to the Examiner's comments, the specification has sufficient disclosure to enable the use of peptides that are deleted and/or substituted

variants of SEQ ID NO: 1. For example, pages 22-27 of the specification set forth specific examples of the deletion type and/or substitution type muteins that can be used in the present invention. See also e.g., pages 119-131. Pages 28-32 of the specification similarly set forth examples of precursors that are useful. In addition, the specification clearly enables the selection of peptides of the present invention, e.g., on pages 83 through 88. Finally, the specification also sets forth specific examples of assays that can be used to measure activity of the selected peptides, precursors and fragments, e.g., at pages 162-168.

The amount of guidance necessary to enable the invention is inversely related to the amount of knowledge and predictability in the state of the art. While the field of the invention may be unpredictable, the Applicants have provided substantial guidance within the specification to clearly enable the claimed invention. Therefore, Applicants respectfully request that this rejection be reconsidered and withdrawn.

Claim 20 stands rejected under 35 USC 112, first paragraph, as non-enabling. Applicants respectfully traverse this rejection.

It is the Examiner's position that even though the specification is enabling for a pharmaceutical composition comprising the amino acid sequence of SEQ ID NO:1 that has sleep modulating activity, it does not enable the uses set forth in claim 20. Applicants respectfully disagree with the Examiner's position. The "Background Art" section of the specification describes the broad distribution of somatostatin and its range of activity, as well as the effects of cortistatin. The Background also lists the types of diseases that can be treated by drugs developed using compounds that have somatostatin or cortistatin activity. In addition, on pages 74-80, and 104-108, the specification sets forth the types of diseases that the peptides of the present invention can be used for treating. Thus, one of ordinary skill in the art can readily utilize the pharmaceutical composition recited in claim 20 for the uses recited therein.

Therefore, Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

Claims 1-8, 18, 20, 24 stand rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey that the inventors had possession of the claimed invention. Applicants respectfully traverse this rejection.

The Examiner acknowledges that the specification discloses SEQ ID NO: 7, which corresponds to the single, full length species of precursor protein and that this SEQ ID NO: meets the written description and enablement provision of 35 USC 112, first paragraph. However, the Examiner argues that the claims are directed to or encompass all precursor proteins, which do not satisfy the written description requirement.

Applicants respectfully disagree with the Examiners' position. The specification describes the precursor proteins covered by the present claims. For example, on pages 28-34, the specification provides numerous examples of precursor proteins and states that the precursor "may be any peptide or protein provided that it contains the above-mentioned peptide [i.e., having SEQ ID NO:1] of the present invention." One of ordinary skill in the art would clearly recognize what is described in the specification, in light of the knowledge in the art. Thus, the claims encompassing the precursor proteins satisfy the written description requirement and Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

Claims 1, 2, 7, 8, 18, 20, 24 stand rejected under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Applicants respectfully submit that the above discussions and claim amendments obviate these rejections.

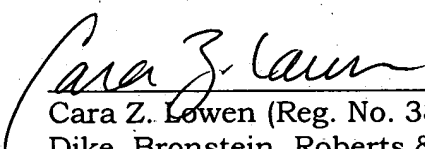
Claim 20 was rejected as is indefinite due to the recitation of "a neural activity or sleep modulator". Applicants respectfully submit that the claim is not indefinite because one of ordinary skill in the art would understand what is meant by this terminology. The specification refers to a journal article describing cortistatin as a "modulator of neural activities and sleep." See page 2, line 13-14. This activity is known in the art and therefore is not indefinite. Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

Claim 6 stands rejected under 35 USC 102(b) as being anticipated by Andrews. Applicants respectfully traverse this rejection. However, Applicants respectfully submit that the above amendments to the claims, which have been made in order to expedite examination of this case, obviate this rejection. Applicants therefore, respectfully request reconsideration and withdrawal of this rejection.

In view of the discussion above, it is respectfully submitted that the present application is in condition for allowance. An early reconsideration and notice of allowance are earnestly solicited. Should the Examiner wish to discuss the above amendment made herein, the undersigned attorney would appreciate the opportunity to do so. Thus the Examiner is hereby invited to call the undersigned, collect at the number shown below.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE.

In the specification:

The following paragraph has been inserted after the title of the invention:

--This application is a continuation in part of PCT/JP97/01911, filed on June 5, 1997, claiming priority from JP146052 (filed on June 7, 1996), JP247710 (filed on September 19, 1996) and JP272422 (filed on October 15, 1996).--

In the claims:

Claims 1, 6, 8 and 20 have been amended as follows:

1. (amended)      A An isolated peptide comprising the amino acid sequence defined under SEQ ID NO: 1 or amino acid sequence derived therefrom by deletion, substitution or insertion of 1 to 5 amino acid residues ~~(except for the amino acid sequence defined under SEQ ID NO: 31 or SEQ ID NO: 32)~~, a precursor thereof, or a salt of said peptide ~~or precursor~~, wherein the peptide does not comprise the amino acid sequence of SEQ ID NO: 31 or SEQ ID NO: 32.

6. (amended)      ~~A peptide as claimed in Claim 1 which comprises~~ An isolated peptide having the amino acid sequence defined under any of SEQ ID NO: 35 through SEQ ID NO: 55, a precursor thereof, or a salt of said peptide.

8.      A peptide or precursor as claimed in Claim 1 which has cortistatin-~~like~~ or somatostatin-~~like~~ activity.

20. A pharmaceutical composition as claimed in Claim 18 ~~or 19~~ which is an agent for the treatment or prevention of hormone producing tumors, acromegaly, giantism, dementia or gastric ulcer, a hormone secretion inhibitor, a tumor growth inhibitor, or a neural activity or sleep modulator.